

**Remarks**

By the foregoing amendment, claims 1 and 7 have been amended and claims 4-6, 9-16 have been canceled. Applicants note that no new matter has been added and support for the amendments can be found throughout the specification. For example, page 6 of the specification at lines 31 to 33 provides support for "stem cells." Support for "autonomically beating cardiac muscle-like cell aggregates" can be found, for example, at line 26 on page 12 of the specification. Support for the amendment of claim 7 regarding the retinoic acid receptor ligand not substantially binding to the retinoic acid receptor subtype  $\gamma$  can be found, for example, on page 3, lines 17-19; page 4, lines 4-5 and 11-12; and page 8, lines 26-28.

**Formal Matters**

Applicants note that the Office Action does not indicate any acknowledgment of the claim for foreign priority under 35 U.S.C § 119 which was filed on September 19, 2005. Applicants respectfully request that an acknowledgment be made with the next communication.

Applicants note with appreciation that the Examiner has considered the materials submitted in the Information Disclosure Statement dated October 2, 2006 and indicated such consideration by returning an electronically signed and initialed copy of the Form PTO-1449.

**Objection to the Claims**

The Action objects to claims 1, 4-6, and 10-16 for the omission the article “a” or “the” before the word “tissue.” In view of the foregoing amendment, Applicants respectfully submit that this rejection is moot. Applicants respectfully request withdrawal.

**Claim Rejections under 35 U.S.C. § 112, first paragraph**

The Action rejects claims 1-16 under 35 U.S.C § 112, first paragraph for allegedly failing to enable a “method for forming an organ, wherein the organ is a heart, a smooth muscle tissue, a pancreas, and an adipocyte tissue in the presence of any retinoic acid X receptor agonist or antagonist.” The Examiner concedes that the claims would enable “a method for forming cardiac muscle-like cell aggregates, smooth muscle cell-like aggregates, adipocytes, and an intestine-like structure from undifferentiated cells.”

With the present amendment, Applicants submit that the claims are fully enabled and respectfully request withdrawal of the enablement rejection.

**Claim Rejection under 35 U.S.C. § 112, second paragraph**

The Office rejects claim 7 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite with respect to the phrase “that does not bind to the retinoic acid receptor subtype  $\gamma$ .” It is allegedly unclear what molecule does not bind to the retinoic acid receptor.

With the present amendment, Applicants respectfully submit that this rejection has been addressed and requests withdrawal thereof.

**Claim Rejections under 35 U.S.C. § 102**

The Office Action raises the following anticipation rejections:

- (a) Claims 1, 2, 5-7, 9, and 12 are rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Moriya et al., Develop. Growth Differ. (2000), vol. 42, pp. 593-602.
- (b) Claims 1, 2, 3, 6, and 9 are rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Takahashi et al., J. Med. Chem. (2002), vol. 45, no. 16, pp. 3327-330.

The Action asserts that Moriya allegedly disclosing the formation of pancreas tissue from undifferentiated cells from *Xenopus* in the presence of all-*trans*-retinoic acid anticipates the recitations of claims 1, 2, 5-7, 9, and 12. As for rejection (b), the Action asserts that Takahashi allegedly disclosing the culturing undifferentiated cells (HL-60) in the presence of an RXR agonist or antagonist, and an differentiation inducer anticipates the recitations of claims 1, 2, 3, 6, and 9.

Applicants respectfully traverse these rejections. Applicants submit that neither Moriya nor Takahashi disclose stem cells forming “autonomically beating cardiac muscle-like cell aggregates” or “a tissue having morphology and function of a pancreas.” The cells from which Moriya forms an *in vitro* pancreas are presumptive ectoderm.

Applicants submit that presumptive ectoderm cells are not stem cells, but rather late stage precursors just before they become differentiated ectoderm cells.

Similarly, in rejection (b), the disclosed human promyelocytic leukemia cells HL-60 are not stem cells.

In view of the foregoing remarks, Applicants respectfully submit that Moriya and Takahashi fail to disclose the invention, at least with respect to the feature of "stem cells" as required by claim 1. Applicants respectfully request withdrawal of the anticipation rejection.

#### **Claim Rejections under 35 U.S.C. § 103**

The Action rejects claims 1-16 under 35 U.S.C. § 103(a) as allegedly being obvious over Moriya in view of Takahashi and in further view of Drysdale et al., *Developmental Biology*, (1997), vol. 188, pp.205-215 and further in view of Neuville et al., *Atheroscler. Thromb. Vasc. Biol.*, (1999), vol. 19, pp. 1430-1436. The Action asserts that all recitations of the rejected claims are present by combining these four documents.

Applicants respectfully traverse this rejection. Applicants note that none of the secondary references cure the deficiencies of Moriya or Takahashi in response to the anticipation rejection because none of the secondary references disclose stem cells. Furthermore, Applicants respectfully submit that none of the asserted combination of the cited documents would give a reason to one of ordinary skill in the art to apply the claimed method on "stem cells." Therefore, Applicants respectfully submit that the cited

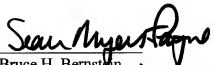
documents, in any combination, fail to render obvious the claimed invention. Withdrawal of the rejection is respectfully requested.

**Conclusion**

Applicants respectfully request reconsideration of the outstanding Office Action and allowance of the present application and all the claims therein.

Should the Examiner have any further comments or questions or if any issues remain which can be expeditiously resolved by a telephone conference, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,  
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